Contemporary Methods Allowing for Safe and Convenient Use of Amniotic Membrane as a Biologic Wound Dressing for Burns

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Abstract: Partial-thickness burns involve damage to the upper layer of skin, which leaves nerve endings exposed, and therefore represent the most painful of several categories of thermal injuries. Historically, partial-thickness burns were treated conservatively by debriding the blisters, by daily tubbing and washing, and the application of new bandages with topical medications. Human amniotic membrane has been used for centuries as a biological wound dressing. In the past 20 years, there has been an increasing body of literature addressing the use of amniotic tissue in chronic wounds and burns. In this review, we present an overview of the use of amniotic membrane in the treatment of burns including processing methods and early clinical use. We believe that amniotic membranes have great potential in improving burn wound care in the future. Standardized processing methods and terminal sterilization ensure safety and allow the material to be available for use by health care providers around the world in clinical trials and for patient care.

Key Words: amnion, human amniotic membrane, partial-thickness burns

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OVERVIEW

Partial-thickness burns involve damage to the upper layer of skin, which leaves nerve endings exposed, and therefore represent the most painful of several categories of thermal injuries. Historically, partial-thickness burns were treated conservatively by debriding the blisters, by daily tubbing and washing, and the application of new bandages with topical medications 2 to 4 times each day. These procedures cause excruciating pain and anxiety in patients even with the use of narcotics. To reduce the pain level, to provide better infection control and faster wound healing, and to minimize the stress level for both patient and nurse, a number of occlusive dressings have been developed in the recent years.[1] These skin substitutes allow reepithelialization to occur underneath and eliminate the need for daily tubbing and frequent dressing changes.

Human amniotic membrane has been used for centuries as a biological wound dressing. In the Far East (China and Japan), placental tissue has been considered a potent medication for the treatment of many diseases and believed to have "magical strength of youth" (quoted by Tyszkiewicz et al[2]). In Western medicine, amniotic membranes have been used since the beginning of the last century. The first reported use of amniotic membrane in burn wounds was by Sabella in 1913,[3] shortly after Davis reported on the use of the material in skin transplantations in 1910.[4] Many advantages of amniotic membrane as a wound dressing have been reported, most notably prevention of infection,[5–8] alleviation of pain,[7,8] acceleration of wound healing,[5,7,9] and good handling properties.[10]

In the past 20 years, there has been an increasing body of literature addressing the use of amniotic membrane in chronic wounds and burns. To make amniotic tissue a standard dressing alternative, safe and reliable production methods had to be implemented.

CLINICAL USE OF AMNIOTIC MEMBRANE

The most important qualities of amniotic membrane include a low antigenicity, good adherence to the wound surface, potential antimicrobial activity, and its abundant availability. Trials have been performed in acute, partial-thickness and full-thickness wounds, and different forms of procurement and storage of amniotic membrane have been reported. Gruss et al[11] showed the benefits of decreasing wound bacterial counts, accelerating wound healing and promoting the growth of granulation tissue over chronic wounds and exposed bones in a cohort of 120 patients. The amniotic membranes used in this study were not separated from the chorion and only processed by repeatedly washing the material, with microbiology cultures used as proof of sterility of the membrane. The authors used the material on ulcers, elective surgical wounds, infected and burn wounds. In a similar trial, Robson and Krizek[6] used amniotic membranes in 150 patients. Thirty years after these initial reports on the use of amniotic membrane, our group[12] studied over 100 patients with partial-thickness burns of the face, neck, and head in a randomized controlled fashion, comparing the use of amnion (n = 53) to topical antimicrobials (n = 49), and assessing multiple clinical variables, such as length of hospital stay, rate of infections, time to total healing, and frequency of dressing changes. Patients in the amnion group had significantly less dressing changes than in the control group, with time to healing, length of stay, and the development of hypertrophic scarring not different between the groups. The use of amnion was not associated with an increased risk of local infection. We concluded that amnion is safe and has advantages as wound coverage for second-degree facial burns compared with the standard topical ointments.

Although these trials certainly provide valuable data and first insights into the potential of amniotic membranes in wound healing, clinicians in the United States today face a much higher threshold for use of human tissue allografts, including ensuring that the material has been processed in a way that excludes potential contamination with human immunodeficiency virus, hepatitis, and herpes viruses. Regulations from the American Association of Tissue Banks require highly regulated processing facilities, and strict procurement and storage rules for amniotic tissue in the United States.

PREPARATION OF AMNIOTIC MEMBRANES FOR CLINICAL USE

Historically, various methods have been used to clean amniotic membranes and maintain their natural properties for clinical use. Haberal et al[13] used 0.5% silver nitrate for over 2 hours; Robson and Krizek[6] used a rinse of 0.025% sodium hypochlorite solution to ensure sterility. Maral et al[5] used glycerol-preserved amnion. Although these techniques may be adequate in certain situations, they lack the ability

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to provide for large quantities of the material to be distributed, stored, and conveniently obtained by clinicians over a widespread area.

More recently, techniques have been developed to make amniotic membrane products commercially available. One such product (EpiFix; AmnioFix; EpiBurn; MiMedx Group, Inc., Marietta, GA) is a dehydrated human amnion/chorion membrane (dHACM). This dHACM allograft is available in multiple sizes and configurations with a 5-year shelf life under ambient conditions. A patented PURION Process of gently cleansing and dehydrating the amniotic membrane collected from screened and tested donors delivering via Caesarean section results in a product with cells that are nonviable, yet retain the cellular and pericellular components essential for biological activity.[14–16] Terminal sterilization of the dHACM allograft tissue reduces the risk for disease transmission, such as Zika, and provides a less than 1 in 1 million probability of a nonsterile unit.

The PURION-Processed dHACM has been shown to contain more than 226 growth factors, chemokines, cytokines, and other regulatory proteins that are important for stimulating and managing the major processes involved in tissue healing, including burn injuries.[14–16] These various growth factors, immunomodulatory cytokines, chemokines, and other proteins have been shown to play important roles in tissue healing and regeneration, and proven to attract stem cells to areas of tissue injury, such cells potentiating the healing processes.[14] PURION-Processed dHACM grafts have concentrations of these factors that generally exceed those of single-layer or multilayer grafts processed by other methods by 20 times or more.[17] These observations support the conclusion that dHACM is potentially a very good alternative to fresh amnion/chorion membranes for treating burn patients.

SUMMARY

There is a considerable amount of literature on use of amniotic membrane in a wide variety of clinical situations over the last century. The body of evidence is being further developed for the use of commercially prepared amniotic membrane products, such as dHACM, and their role in treating thermal injuries. We believe that amniotic membranes have great potential in improving burn wound care in the future. Commercial availability of products such as dHACM allows for wider and more convenient use of amniotic membrane in a variety of clinical settings. Further clinical trials should lead to more standardized protocols for their use, document application methods, and further confirm safety.

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